REMARKS

This Amendment is in response to the Examiner's Final Office Action mailed on November 17, 2004. Claims 23-80 have been canceled without prejudice. Claim 1 has been amended. Claims 1-22 are now pending.

Applicants express their appreciation to Examiner Epperson for conducting a telephone interview with Applicants on February 23, 2005. During the interview, the issues of patentability of the pending claims were discussed. Applicants' remarks on each issue raised in the Office Action are presented below.

I. Rejection Under 35 U.S.C. §112, First Paragraph

Claims 1-22 stand rejected under 35 U.S.C. §112, first paragraph for failing to comply with the written description requirement. The Examiner based the rejection on the court decision of *The Regents of the University of California vs. Eli Lilly and Company 119 F.3d 1559 (Fed. Cir., 1997)*. Specifically, the Examiner states that "the instant claims define the components of the claimed library only by their functional definition insufficient to adequately describe the claimed product." The Examiner further stated that when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

During the interview, Applicants distinguished the claimed library with the claimed nucleotide sequence encoding human insulin in *Eli Lilly*. In *Eli Lilly* Applicants claimed cDNA encoding human insulin without providing the actual cDNA sequence in the specification. In contrast, each nucleic acid construct of the library in the present invention is readily ascertainable and adequately described in the Specification. As recited in independent claim 1, each nucleic acid in the construct comprises i) a cis element sequence comprising one or more copies of a cis element to which a transcription factor is known to bind, the cis element sequence varying within the library of nucleic acid constructs; ii) a promoter sequence **3' relative to the cis element sequence**; and iii) a reporter sequence **3' relative to the promoter sequence** that comprises a variable sequence that varies within the library of nucleic acid constructs. The cis element in each construct corresponds to a given reporter sequence within the library of nucleic

acid constructs. Thus, claim 1 not only recites **each element** comprised in the each of the constructs in the library but also defines the **structure** of the nucleic acid construct.

Further, pursuant to MPEP §2163.05I, "[t]he written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species" which means that the species which are adequately described are representative of the entire genus. In the instant application, the Specification not only provides ample examples of what the library is but also teaches how to construct the library of nucleic acid constructs comprising various cis elements known to bind to various transcription factors. Applicants respectfully direct the Examiner's attention to pages 13-16, a section under "DETAILED DESCRIPTION OF THE INVENTION", and Figures 1A, 1B, and 2. In particular, the table in Figure 2 lists 30 examples of cis elements (listed under the column labeled as "Cis-Element") that are known to bind to transcription factors (listed under the column labeled as "Transcription Factor"). Numerous example of the promoter sequence are also listed on page 18, lines 17-20. The Specification further describes how to construct the library of nucleic acid constructs in the section entitled "Libraries Comprising Cis Element – Reporter Sequence Constructs", pp. 16-20. For example, the Specification teaches that the cis element is included in the construct 5' relative to the promoter (page 18, lines 13-14) and the reporter is positioned 3'relative to the promoter (page 18, lines 23-24); and binding transcription factors to the cis elements results in the reporter sequence being transcribed to produce mRNA (page 18, lines 23-25). Thus, to one of ordinary skill in the relevant art, the detailed description and ample examples provided in the specification should be sufficient to show that the inventors, at the time the application was filed, had possession of the claimed invention.

In the determination of whether the claimed invention has met the written description requirement, the burden is on the Examiner to inquire on a factual or case-by-case basis. "A description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. In rejecting a claim, the examiner must set forth express findings of fact which support the lack of written description conclusion." MPEP 2163.04.

In support the rejection, the Examiner stated that there is not a single working example of the claimed invention. However, the Examiner ignored the extensive teaching of each of the elements and how to construct the library in the Specification. And the Examiner has not provided sufficient evidence or reasoning why the numerous examples described in the specification are not a representative number of species and why the teaching in the specification is insufficient to demonstrate that the inventors had the inventors, at the time the application was filed, had possession of the claimed library of nucleic acid construct.

Absent factual evidence to the contrary, the rejection of the claims for lack of written description is not legally supported under 35 U.S.C. §112, First Paragraph. Withdrawal of rejection is therefore respectfully requested.

II. Rejection Under 35 U.S.C. §112, First Paragraph — New Rejections

The Examiner further rejected claim 1 under 35 U.S.C. §112, First Paragraph for containing new matter.

Claim 1 as amended specifies that each construct comprises a cis element sequence which includes one or more copies of a cis element to which a transcription factor is known to bind; and the cis element sequence varies within the library of nucleic acid constructs. Support for the claim language appears in the Specification, for example, at page 17, lines 3-4.

The Examiner also rejected claim 1 for containing new matter as to the phase "a reporter sequence that is 3' relative to the promoter sequence and comprises a variable sequence that varies within the library of nucleic acid constructs." Applicants amend claim 1 to specify "a reporter sequence 3' relative to the promoter sequence, the reporter sequence comprising a variable sequence that varies within the library of nucleic acid constructs." Support for the claim language appears in the Specification, for example, at page 7, lines 25-26.

In view of the above amendments and remarks, Applicants submit that claim 1 has adequate written support in the specification as originally filed under 35 U.S.C. §112, First Paragraph. Withdrawal of rejection is therefore respectfully requested.

III. Rejection Under 35 U.S.C. §102(b)

Claims 1-13 and 20 stand rejected under 35 U.S.C. §102(b) as being anticipated by Kauffmann et al. (WO 00/04196).

Independent claim 1 as amended specifies a library of nucleic acid constructs each of which comprises i) a cis element sequence comprising one or more copies of **a cis element to which a transcription factor is known to bind**, the cis element sequence varying within the library of nucleic acid constructs; ii) a promoter sequence 3' relative to the cis element sequence; and iii) **a reporter sequence** that is 3' relative to the promoter sequence and comprises a **variable sequence that varies within the library of nucleic acid constructs**. The cis element in each construct corresponds to a given reporter sequence within the library of nucleic acid constructs.

As discussed during the interview, Kauffmann et al. neither teaches nor suggests such a claimed library of nucleic acid construct. In contrast, Kauffmann et al. teaches a method of **identifying nucleic acid molecules that contain cis acting nucleic acid elements**. *See* Abstract. According to Kauffmann et al. the invention is to provide a solution to the problems existing in the art. Kauffmann et al. points out that "[a]t present... there is no broadly applicable method to identify cis acting nucleic acid elements **without prior identification of the regulated nucleic acid or of the regulatory nucleic acid binding factor**." Page 3, lines 5-11. To find cis acting nucleic acid elements in a diverse library of nucleic acid candidate molecules, a diverse population of nucleic acid molecules are used which comprise a plurality of different isolated polynucleotide nucleic acid molecules that **potentially** contain cis acting elements. Page 11, lines 27-29. Thus, this reference teaches a library of nucleic acid molecules some of which **might be** a cis element or cis elements after the screening assay. Therefore, Kauffmann et al. fails to teach the claimed library of nucleic acid construct each of which comprises one or more copies of **a cis element to which a transcription factor is already known to bind**.

Further, Kauffman et al. also fails to teach a library of nucleic acid constructs each of which comprises **a reporter sequence** that is 3' relative to the promoter sequence and comprises **a variable sequence that varies within the library of nucleic acid constructs**. Kauffman et al.

merely discloses that "if desired, some or all of the isolated nucleic acid molecules can ... be flanked at one or both ends by ... detectable sequences, such as sequences homologous to oligonucleotide primers for the polymerase chain reaction (PCR), sequence containing restriction sites, or detectable sequence." Nowhere does this reference teach or suggest a library of nucleic acid constructs having a reporter sequence 3' relative to the promoter sequence which is **3' relative to the cis element AND varies within the library**.

In view of the structural and functional distinction between the claimed invention and the disclosure of Kaufmann et al., Applicants submit that claims 1-22 are not anticipated by Kauffmann et al. under 35 U.S.C. §102(b). Withdrawal of this ground of rejection is therefore respectfully requested.

IV. Rejection Under 35 U.S.C. §103(a)

Claims 1-22 stand rejected under 35 U.S.C. §103(a) as being anticipated by Kauffmann et al. (WO 00/04196) and Morris et al. (U.S. Patent No. 6,458,530).

As discussed in detail above, Kauffmann et al. fails to teach the claimed library of nucleic acid construct each of which comprises one or more copies of a cis element to which a transcription factor is already known to bind; and a reporter sequence 3' relative to the promoter sequence and varies within the library.

On the other hand, Morris et al. discloses methods of selecting tag nucleic acids and VLSIPS™ arrays and **the arrays made by the methods are used to label and track compositions**, including cells and viruses. *See* Abstract. Nowhere does Morris et al. teach or suggest the claimed library of nucleic acid constructs each of which comprises i) a cis element sequence comprising one or more copies of a cis element to which a transcription factor is known to bind, the cis element sequence varying within the library of nucleic acid constructs; ii) a promoter sequence 3' relative to the cis element sequence; and iii) a reporter sequence that is 3' relative to the promoter sequence and comprises a variable sequence that varies within the library of nucleic acid constructs.

To establish a prima facie case of obviousness, the Examiner bears the burden of proving 1) the prior art reference (or references when combined) must teach or suggest all of the claim limitations; 2) the prior art contains a suggestion or motivation to combine the prior art references in such a way as to achieve the claimed invention; and 3) one of ordinary skill in the art at the time the invention was made would have reasonable expectation of success of the claimed invention. *In re Vaeck*, 947 F. 2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991); *In re O'Farrell*, 853 F. 2d 894, 903-904, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988); and *In re Dow Chem.*, 837 F. 2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988).

There is not motivation to combine the teaching of Kauffmann et al. and Morris et al. to arrive at the present invention. Kauffmann et al. teaches a method for identifying **new** cis elements from a diverse library of nucleic acid candidates. If a library of nucleic acid constructs each of which comprises one or more copies of a cis element to which a transcription factor is **already known** to bind, Kauffmann's purpose of finding new cis elements would have been defeated. In addition, Morris et al. focused on selecting tag nucleic acids that "have uniform hybridization characteristics (i.e., similar thermal binding stability to complementary nucleic acids), making the tag sets suitable for detection by VLSIPS™ and other probe arrays, such as Southern or northern blots." See Summary of Invention; column 12, lines 65-67 and column 13, lines 1-2. Thus, linking a variable cis element to the tag nucleic acid would not only render the method inoperable due to complication of dual variables, but also defeat the purpose of selecting tags with desirable characteristics. In view of these disadvantages, one of ordinary skill in the art would not be motivated to modify Kauffmann et al. in view of Morris et al. or vice versa to arrive at the claimed invention.

Based on the reasons set forth above, Applicants submit that a prima facie case of obviousness has not been established under 35 U.S.C. §103(a). Withdrawal of this ground of rejection is therefore respectfully requested.

CONCLUSION

In light of the remarks and arguments set forth above, Applicants earnestly believe that they are entitled to a letters patent, and respectfully solicit the Examiner to expedite prosecution of this patent application to issuance. Should the Examiner have any questions, the Examiner is encouraged to telephone the undersigned.

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Respectfully submitted,

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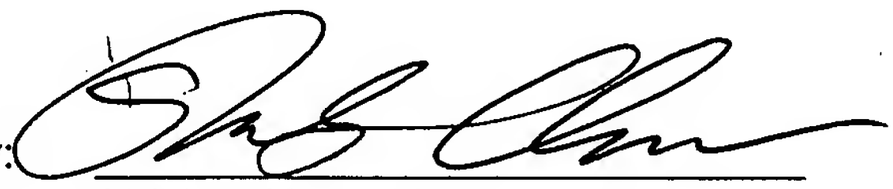
By: 

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